In the claims

Please cancel claims 2-3, 5-8, 10, 17-19, 21, 29-33, 37-39 and 42-44 without prejudice.

Please amend claims 1, 9, 11-14, 16, 20, 24, 25, 28 34-36 and 40 as follows:

1. (Currently Amended) A method of diagnosing ~~a cellular proliferative disorder of breast tissue~~ primary breast cancer in a subject comprising determining the state of methylation of one or more CpG islands in the promoter of RAR β2 nucleic acids isolated from a sample comprising blood, plasma, lymph, duct cells, ductal lavage fluid, nipple aspiration fluid, breast tissue, lymph nodes, bone marrow, or a combination thereof of the subject, wherein [[the]] a state of hypermethylation of one or more CpG islands in the promoter of RAR β2 nucleic acids as compared with the state of methylation of one or more CpG islands in the promoter of RAR β2 nucleic acids in comparable samples obtained from ~~a subject not having the cellular proliferative disorder of breast tissue~~ normal subjects is indicative of ~~a cellular proliferative disorder of breast tissue~~ primary breast cancer in the subject.

Claims 2-3. (Cancelled)

4. (Original) The method of claim 1, wherein the state of methylation of the nucleic acids is determined simultaneously.

Claims 5-8 (Cancelled)

9. (Currently Amended) The method of claim [[6]] 1, wherein the sample comprises duct cells ~~are~~ obtained by a procedure selected from ductal lavage, sentinel node biopsy, fine needle aspirate, routine operative breast endoscopy, nipple aspiration and core biopsy.

10. (Cancelled)

11. (Currently Amended) The method of claim [[2]] 1, wherein determining the state of methylation comprises amplifying the nucleic acid by means of at least one sense primer and at least one antisense primer that distinguishes between methylated and unmethylated nucleic acids.

12. (Currently Amended) The method of claim 11, wherein the primers hybridize with target polynucleotide sequences selected from SEQ ID NO:~~1-4, 15-18,~~25-36, 41-48, ~~65-66, 73-76, 81-82, 111-115, 122-123~~, and combinations thereof.

13. (Currently Amended) The method of claim 11, wherein the primers are selected from SEQ ID NO:~~7-14,~~21-24, 37-40, ~~49-64, 69-72, 77-80, 85-90, 116-119, 124-128~~, and combinations thereof.

14. (Currently Amended) The method of claim [[2]] 1, further comprising contacting the nucleic acid with a methylation-sensitive restriction endonuclease.

15. (Original) The method of claim 14, wherein the methylation-sensitive restriction endonuclease is selected from the group consisting of MspI, HpaII, BssHII, BstUI and NotI.

16. (Currently Amended) A method of determining a predisposition to ~~a cellular proliferative disorder of breast tissue~~ primary breast cancer in a subject comprising determining the state of methylation of one or more CpG islands in the promoter of RARβ2 nucleic acids isolated from a sample comprising blood, plasma, duct cells lymph, ductal lavage fluid, nipple aspiration fluid, breast tissue, lymph nodes bone marrow, or a combination thereof of the subject,

~~wherein the nucleic acid is selected from the group consisting of Twist, cyclin D2, RARβ2, HOXA5, WT1, 14.3.3 sigma, estrogen receptor, NES-1, RASSF1A, HIN-1 and combinations thereof; and~~

wherein [[the]] a state of hypermethylation of the CpG islands in the promoter of RAR β2 nucleic acid(s) as compared with the state of methylation of comparable nucleic acid obtained from ~~a subject not having the predisposition to the cellular proliferative disorder of breast tissue~~ normal subjects is ~~hypermethylation and~~ indicative of ~~a cellular proliferative disorder of breast tissue~~ a predisposition to primary breast cancer in the subject.

Claims 17-19. (Cancelled)

20. (Currently Amended) The method of claim [[19]] 16, wherein the sample comprises duct cells [[are]] obtained by a procedure selected from the group consisting of ductal lavage, sentinel node biopsy, fine needle aspirate, routine operative breast endoscopy, nipple aspiration and core biopsy.

21. (Cancelled)

22. (Original) The method of claim 16, wherein determining the state of methylation comprises amplifying the nucleic acid(s) by means of at least one sense primer and at least one antisense primer that distinguishes between methylated and unmethylated nucleic acid.

23. (Original) The method of claim 22, wherein the nucleic acids are amplified simultaneously.

24. (Currently Amended) The method of claim 22, wherein the primers hybridize with target polynucleotide sequences selected from SEQ ID NO:~~1-4, 15-18,~~25-36, 41-48, ~~65-66, 73-76, 81-82, 111-115, 122-123~~, and combinations thereof.

25. (Currently Amended) The method of claim 24, wherein the primers are selected from SEQ ID NO:~~7-14,~~21-24, 37-40, ~~49-64, 69-72, 77-80, 85-90, 116-119, 124-128~~, and combinations thereof.

26. (Original) The method of claim 16, further comprising contacting the nucleic acid with a methylation-sensitive restriction endonuclease.

27. (Original) The method of claim 26, wherein the methylation-sensitive restriction endonuclease is selected from the group consisting of MspI, HpaII, BssHII, BstUI and NotI.

28. (Currently Amended) A method for diagnosing ~~a cellular proliferative disorder of breast tissue~~ primary breast cancer in a subject comprising:

(a) contacting a nucleic acid-containing specimen selected from blood, plasma, lymph, duct cells, ductal lavage fluid, nipple aspiration fluid, breast tissue, lymph nodes bone marrow, or a combination thereof of the subject with an agent that provides a determination of the methylation state of CpG islands in the promoter of RARβ2 nucleic acids in the specimen, and

(b) identifying the methylation state of at least one ~~region of least one nucleic acid~~ CpG island in the promoter of RARβ2, wherein the CpG islands in the promoter of RARβ2 ~~of least one nucleic acid methylation state of at least one region of at least one nucleic acid that~~ is ~~different from~~ hypermethylated compared to the methylation state of the same region of the same nucleic acid in ~~a subject not having the cellular proliferative disorder is indicative of a cellular proliferative disorder of breast tissue in the subject~~ normal subjects.

Claims 29-33. (Cancelled) .

34. (Currently Amended) The method of claim [[30]] 28, wherein the agent is at least one sense primer and at least one antisense primer that hybridize with a target sequence in the nucleic acid.

35. (Currently Amended) The method of claim 34, wherein the primers hybridize with target polynucleotide sequences selected from SEQ ID NO:~~1-4, 15-18,~~ 25-36, 41-48, ~~65-66, 73-76, 81-82, 111-115, 122-123~~, and combinations thereof.

36. (Currently Amended) The method of claim 34, wherein the primers are selected from SEQ ID NO:~~7-14,~~ 21-24, 37-40, ~~49-64, 69-72, 77-80, 85-90, 116-119, 124-128~~, and combinations thereof.

Claims 37-39 (Cancelled)

40. (Currently Amended) The method of claim [[39]] 34, wherein the method employs multiplex methylation-specific PCR.

41. (Original) The method of claim 40, wherein the specimen comprises breast duct or ductal fluid.

Claims 42-44 (Cancelled)